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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/913,559	02/08/2002	Eric F. Bernstein	BERN-0050	2377

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EXAMINER	
PARAS JR, PETER	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/913,559	BERNSTEIN, ERIC F.	
	Examin r	Art Unit	
	Peter Paras, Jr.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-6 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-6 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 0801 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-6 are pending and are under current consideration.

Specification

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a transgenic hairless mouse capable of expressing a full length or truncated human elastin promoter. The claims are further directed to methods of screening compounds using the same transgenic mouse, fibroblast cultures derived from the same transgenic mouse, and methods of screening compounds using the same fibroblasts.

The specification discusses that the invention features a transgenic mouse capable of expressing a human elastin promoter. See page 4. The specification

discusses that the invention features investigation of human elastin promoter activity in response to ultraviolet irradiation both *in vivo* by direct irradiation of mouse skin and *in vitro* by irradiation of dermal fibroblasts obtained from the same mouse. While the specification provides extensive teachings, specific guidance, and working examples pertaining to the creation of a transgenic mouse whose genome comprises a homozygous full-length human elastin promoter operably linked to a nucleotide sequence encoding a reporter protein, wherein the reporter protein is expressed in the skin of said transgenic mouse, fibroblasts obtained from the same mouse, and methods of the mouse and/or the fibroblasts for identifying compounds capable of inhibiting cutaneous photodamage or oxidative damage, the specification fails to provide any relevant teachings or specific guidance with regard to the generation of the other transgenic mice embraced by the claims and their corresponding phenotypes. In view of the lack of guidance provided by the specification it would have required undue experimentation to make and use the other transgenic mice as claimed.

While the specification has provided guidance and working examples directed to the creation of a transgenic mouse whose genome comprises a homozygous full-length human elastin promoter operably linked to a nucleotide sequence encoding a reporter protein the specification fails to provide any relevant teachings, guidance, working examples with regard to the production of the other transgenic mice as claimed. One of skill would not be able to rely on the state of the transgenic art for an attempt to produce the other transgenic mice embraced by the claims. This is because the state of the art of transgenics is not a predictable art with respect to transgene behavior and the

resulting phenotype; the phenotype of the instantly claimed transgenic mice appears to be expression of a reporter protein in the skin; the fact that the claimed mice are hairless is not a result of transgene expression but is due to the age of the mice. While the state of the art of transgenics is such that one of skill in the art would be able to produce transgenic animals comprising a transgene of interest, it is not predictable if the transgene would be expressed at a level and specificity sufficient to cause a particular phenotype. For instance, the level and specificity of expression of a transgene as well as the resulting phenotype of the transgenic animal are directly dependent on the specific transgene construct. The individual gene of interest, promoter, enhancer, coding, or non-coding sequences present in the transgene construct, the specificity of transgene integration into the genome, for example, are all important factors in controlling the expression of a transgene in the production of transgenic animal which exhibits a resulting phenotype. This observation is supported by Wall (Theriogenology, 1996) who states that "[o]ur lack of understanding of essential genetic control elements makes it difficult to design transgenes with predictable behavior." See page 61, last paragraph. See also Houdebine (Journal of Biotechnology, 1994) who discloses that in the field of transgenics, constructs must be designed case by case without general rules to obtain good expression of a transgene (page 275, column 1, 1st paragraph); *e.g.*, specific promoters, presence or absence of introns, *etc.* The breadth of the claims embraces mice that are heterozygous for the transgene as well as mice that are chimeric. However, the guidance and working examples provided by the instant specification exemplify the creation and use of homozygous mice. It would be

unpredictable if heterozygous and chimeric mice would express the transgene at levels sufficient for identifying compounds that can inhibit cutaneous photodamage or oxidative damage. The cells of a heterozygous mouse would only comprise a single copy of the transgene while the cells of a chimeric mouse would randomly comprise single copies of a transgene. A chimeric mouse would not necessarily transmit a transgene through the germline, which means that mice for use in the claimed screening methods would need to be produced continually with no expectation of obtaining uniform transgene expression levels. As such guidance is lacking in the instant specification for the production and use of the other transgenic mice embraced by the claims.

Therefore, in view of the quantity of experimentation necessary to determine the parameters listed above for the production of transgenic mice, the lack of direction or guidance provided by the specification for the production and use of the other transgenic mice embraced by the claims, the absence of working examples for the demonstration or correlation to the production and use of the other transgenic mice embraced by the claims, the unpredictable state of the art with respect to transgene behavior in transgenic mice, and the breadth of the claims drawn to heterozygous and chimeric mice, it would have required undue experimentation for one skilled in the art to make and/or use the claimed invention.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a transgenic hairless mouse capable of expressing a full length or truncated human elastin promoter. The claims are further directed to methods of screening compounds using the same transgenic mouse, fibroblast cultures derived from the same transgenic mouse, and methods of screening compounds using the same fibroblasts.

The nucleotide sequences of all truncated human elastin promoters encompassed within the genus of human elastin promoters have not been disclosed. Based upon the prior art there is expected to be variation among the species of DNA having human elastin promoter activity, because the sequence of human elastin promoters would be expected to vary among individuals. The specification discloses a full-length human elastin promoter but does not disclose any truncated forms of human elastin promoters. There is no evidence on the record of a relationship between the structure of any human elastin promoter and the claimed truncated elastin promoter that would provide any reliable information about the structure of elastin promoters within the genus. There is no evidence on the record that the truncated human elastin promoters had a known structural relationship to any other human elastin promoter. There is no evidence of record that would indicate that any of the claimed truncated human elastin

promoters even have the biological activity of a full-length elastin promoter. In view of the above considerations one of skill in the art would not recognize that applicant was in possession of the necessary common features or attributes possessed by member of the genus, because a full-length elastin promoter is not representative of the claimed genus. Consequently, since Applicant was in possession of only the full-length elastin promoter and since the art recognized variation among the species of the genus of nucleotide sequences having elastin promoter activity, the human full-length elastin promoter was not representative of the claimed genus. Therefore, Applicant was not in possession of the genus of human elastin promoters as encompassed by the claims. University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that to fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention."

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite as written. The claim is directed to a transgenic mouse capable of expressing an elastin promoter. It is well-known in the field of Molecular

Biology that a promoter is not expressed but rather a promoter directs expression of a coding nucleotide sequence. Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term promoter is indefinite because the specification does not clearly redefine the term.

Claim 1 is indefinite as written. The claim recites "capable of" language. Such language is indefinite because it implies a latent potential but does not necessarily require function. Appropriate correction is required.

It is noted that the following claim language may be sufficient to overcome all of the previous rejection under 35 U.S.C. 112, first and second paragraphs: A transgenic hairless mouse whose genome comprises a homozygous full-length elastin promoter operably linked a nucleotide sequence encoding a reporter protein, wherein the reporter protein is expressed in the skin of said transgenic mouse.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Bernstein et al (US 5,648,061).

The claims are directed to a transgenic hairless mouse capable of expressing a full length or truncated human elastin promoter. The claims are further directed to methods of screening compounds using the same transgenic mouse, fibroblast cultures derived from the same transgenic mouse, and methods of screening compounds using the same fibroblasts.

Bernstein et al teach a transgenic hairless mouse capable of expressing a full-length or truncated human elastin promoter and fibroblast cultures obtained from the same transgenic mouse. See columns 5-6 as well as the claims. Bernstein et al also teach methods of identifying compounds capable of inhibiting cutaneous photodamage in either the same mouse or fibroblasts obtained from the same mouse comprising contacting either the mouse or fibroblasts with a test compound, exposing the mouse or fibroblasts with UVA or UVB radiation and measuring human elastin promoter activity. See examples 3-5 in columns 5-6. Finally the teachings of Bernstein et al anticipate claim 5 by disclosing the components of the system. Bernstein et al teach cultured fibroblasts obtained from said transgenic mouse and a means for generating reactive oxygen species within the fibroblast culture, the means being UV irradiation.

Thus, the teachings of Bernstein et al meet all of the instant claim limitations.

Claims 1-5 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Bernstein et al (J. Invest. Dermatol., 1995, 105: 269-273; IDS).

The claims are directed to a transgenic hairless mouse capable of expressing a full length or truncated human elastin promoter. The claims are further directed to methods of screening compounds using the same transgenic mouse, fibroblast cultures derived from the same transgenic mouse, and methods of screening compounds using the same fibroblasts.

Bernstein et al teach a transgenic hairless mouse capable of expressing a full-length or truncated human elastin promoter and fibroblast cultures obtained from the same transgenic mouse. Bernstein et al also teach methods of identifying compounds capable of inhibiting cutaneous photodamage in either the same mouse or fibroblasts obtained from the same mouse comprising contacting either the mouse or fibroblasts with a test compound, exposing the mouse or fibroblasts with UVA or UVB radiation and measuring human elastin promoter activity. Finally the teachings of Bernstein et al anticipate claim 5 by disclosing the components of the system. Bernstein et al teach cultured fibroblasts obtained from said transgenic mouse and a means for generating reactive oxygen species within the fibroblast culture, the means being UV irradiation. See throughout the entire document.

Thus, the teachings of Bernstein et al meet all of the instant claim limitations.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. Patent No. 5,648,061. Although the conflicting claims are not identical, they are not patentably distinct from each other because they both embrace a transgenic mouse comprising a human elastin promoter, fibroblast cultures obtained from the same transgenic mouse, and methods of identifying compounds capable of inhibiting cutaneous photodamage using either the same mouse or fibroblasts obtained therefrom. Although the claims of 5,648,061 do not claim the transgenic mouse as a product, they do require use of the transgenic mouse (or fibroblasts obtained therefrom) for practice of the claimed methods. Accordingly, it would have been obvious to create the transgenic mouse (or fibroblasts obtained therefrom) given the teachings of US 5,648,061.

Therefore the claims of US 5,648,061 would anticipate the claims of the instant application.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is 703-308-8340. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at 703-305-4051. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Official Fax Center number is (703) 872-9306.

Inquiries of a general nature or relating to the status of the application should be directed to Dianiece Jacobs whose telephone number is (703) 305-3388.

Peter Paras, Jr.

Art Unit 1632

PETER PARAS
PATENT EXAMINER

John J. Doll, Director
Technology Center 1600